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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/781,825	02/20/2004	Michel Schneider	1201-98	3965

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EXAMINER	
RAMACHANDRAN, UMAMAHESWARI	
ART UNIT	PAPER NUMBER
1617	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/08/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

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Office Action Summary	Application No.	Applicant(s)	
	10/781,825	SCHNEIDER ET AL.	
	Examiner	Art Unit	
	Umamaheswari Ramachandran	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *61-86* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *61-86* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 2/20/2004
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-60 are canceled and claims 61-86 are pending.

Effective Priority Date

Applicant is informed that in order to receive the benefit of an earlier filing Applicant must first convey the inventive concept of the claim as a whole consistent with the requirements of the USC § 112 first paragraph. Accordingly, the parent cases must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, that the inventor was in possession of the invention. MPEP 2163.05 (I). In the instant case, the claimed dry formulations wherein microbubbles comprise SF6 and the straight chain saturated fatty acid is arachidic, behenic or lignoceric acid, was not disclosed in the parent cases. Accordingly, the effective priority date of the instant application is January 29, 2001, because the invention as a whole was first disclosed at this date.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 61-86 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. 5,380,519 and claims

1-50 of U.S. 6,110,443. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to dry formulations comprising a phospholipid, a stabilizing polymer and gaseous microbubbles.

The patented claims differ as they do not explicitly teach the instant concentrations of phospholipids, however, it would have been obvious to one of ordinary skill in the art at the time of invention to optimize the phospholipid concentrations of the patented claims in order to practice the instant invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 61-86 are rejected under 35 U.S.C. 103(a) as being unpatentable over Beller et al (U.S. 5,599,523) in view of Unger et al (U.S. 5,542,935), Klaveness (U.S. 5,529,766) and Quay (U.S. 5,393,424).

Belier teaches echo contrast agent comprising a gas, anionic phospholipid and polyoxyethylene/polyoxypropylene polymer, for stabilizing micro gas bubbles (see abstract). Belier uses anionic phospholipids such as DPPG or DSPG in amounts of about 0.01 to about 5% (see col 1, lines 55-59). Beller's microbubbles does not contain fatty acid. Further, Belier does not explicitly teach freeze-dried formulations containing SF6.

Unger teaches the use of fatty acids such as palmitic acid in preparing more stable microspheres. Unger also teaches that it is well understood by one skilled in the art that the lipids or liposomes may be manipulated prior and subsequent to being subjected to the methods of the present invention. For example, Unger states that the lipid may be hydrated and then lyophilized, or processed through freeze and thaw cycles, or simply hydrated prior to the formation of gaseous microspheres (col 40, lines 5-25). The reference also teaches that the particular lipids such as fatty acids are chosen to optimize the desired properties, e.g., short plasma half-life versus long plasma half-life for maximal serum stability. Finally, Unger teaches the use of Sulfur hexafluoride as a suitable gas (see col 67, lines 8-13). Unger further teaches the method of administering the therapeutic containing microspheres to a patient and monitoring the microspheres in the region using ultrasound (col. 34, lines 1-8).

Klaveness complement the teachings of Unger by providing the use of polymeric microbubbles that can contain sulfur hexafluoride (abstract, claims 1-10). Similarly, Quay indicates the advantages of using such gases that have a Q coefficient higher than 30 (col 10-14). Sulfur hexafluoride has a Q value of 722 (col 14, table II).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time of invention to modify Beller's microbubbles and incorporate a fatty acid such as palmitic acid, as suggested by Unger, and then employ sulfur hexafluoride, as the gas of choice, because as suggested by Unger, and recommended by Klaveness and Quay, the ordinary artisan would have had a reasonable expectation of success in improving the utility of Beller's microbubbles in ultrasound imaging. Also, Unger teaches that the

particular lipids such as fatty acids are chosen to optimize the desired properties, e.g., short plasma half-life versus long plasma half-life for maximal serum stability Furthermore, as suggested by Unger, methods of Freeze drying microbubble formulations is conventional in the art, and it would have been obvious to one of ordinary skill in the art at the time of invention to prepare a freeze dried formulation of Belier prior to use, because the ordinary artisan would have expected improved stability and ease of storage.

Beller et al, Unger et al , Klaveness and Quay do not teach the weight ratios of fatty acid.

The examiner respectfully points out the following from MPEP 2144.05: "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." I*n re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); *In re Hoeschele*, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969); Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); *In re Kulling*, 897 F.2d 1147, 14 USPQ2d 1056 (Fed.Cir. 1990); and *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997).

Conclusion

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Umamaheswari Ramachandran whose telephone number is 571-272-9926. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER